ORIGINAL RESEARCH

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Comparison of Compounded Deslorelin and hCG for Induction of Ovulation in Mares

P.M. McCue, DVM, PhD, C. Magee, DVM, and E.K. Gee, BVSc, PhD

ABSTRACT

Ovulation-inducing agents are routinely used in broodmare practice. The objective of this study was to compare the efficacy of two compounded deslorelin products and human chorionic gonadotropin (hCG) in inducing ovulation in a clinical reproduction program. Breeding records of 203 mares administered an ovulation-inducing agent during the 2006 breeding season were reviewed. Estrous cycles were included for comparison if agents were administered when the largest follicle was 35 to 45 mm in diameter and endometrial edema was present. There was no significant difference ($P > .05$) in interval to ovulation for mares receiving deslorelin (1.9 ± 0.7 days) or hCG (2.0 ± 0.7 days). The percentage of mares that ovulated within 48 hours after treatment was also not significantly different between the agents (90.1% and 88.3%, respectively). In summary, clinical efficacy at inducing a timed ovulation in estrual mares with follicles 35 to 45 mm was similar between compounded deslorelin and hCG.

Keywords: Ovulation; Induction; Mare; hCG; Deslorelin

INTRODUCTION

An ovulation-inducing agent is commonly administered to mares in estrus to stimulate ovulation within a defined period. Clinical uses may include reproductive management of mares for scheduled mating or timed inseminations with fresh, cooled, or frozen semen.[1-3]

Hormonal agents used for induction of ovulation include human chorionic gonadotropin (hCG), gonadotropin-releasing hormone (GnRH) agonists, and more recently, recombinant equine luteinizing hormone (reLH).[4-6] Selection of a specific agent may be based on cost, efficacy, time of year, age of the mare, follicle size, previous use or success of an ovulation-inducing agent, and clinician preference.

Human chorionic gonadotropin binds to the equine LH receptor in gonadal tissue.[7] The "LH-like bioactivity" of hCG causes maturation and ovulation of the dominant follicle of mares in estrus.[6] Agonists of GnRH, such as deslorelin acetate, stimulate release of endogenous LH and follicle-stimulating hormone from the anterior pituitary.[4,8] The induced surge of LH stimulates follicle maturation and ovulation.

The objective of this study was to compare efficacy of 2 compounded deslorelin products and hCG in inducing ovulation of mares in a clinical reproduction program.

MATERIALS AND METHODS

Breeding records of 203 mares managed at the Equine Reproduction Laboratory, Colorado State University that received an ovulation-inducing agent in 2006 were reviewed. Mares ranged in age from 2 to 25 years and were predominantly of American Quarter Horse, American Paint Horse, and Arabian breeds.

Mares were administered hCG or 1 of 2 compounded deslorelin products to induce ovulation as part of routine breeding management procedures. Data collected included mare age, ovulation-inducing agent used, date of treatment, diameter of the dominant follicle, and endometrial edema score at the time of treatment, date of subsequent ovulation, and interval from treatment to ovulation. An accurate history of previous administration of ovulation-inducing agents was not available for most mares.

Criteria for inclusion in this study were (1) the agent was administered when a follicle 35 to 45 mm in diameter and endometrial edema were both present; and (2) a treated mare must have been examined at least once daily by transrectal ultrasonography from the date of hormone administration until ovulation was detected or until the fate of the dominant follicle was confirmed. Mares administered an ovulation-inducing agent during the transition period were not included in the analysis (ie, all mares had at least 1 documented ovulation before hormone therapy). Mares with follicles <35 mm or >45 mm at time of treatment also were not included in the analysis. Degree of endometrial edema was evaluated using a scoring system of 0 to 3, with specific scoring of 0 = no edema; 1 = smallest amount of edema detectable; 2 = moderate edema throughout the uterus; and 3 = obvious edema throughout the uterus.[9]

Ovulation-inducing agents used were: (a) human chorionic gonadotropin (hCG; Chorulon®; Intervet Inc., Millsboro, DE) at a dose of 2,500 IU, administered intravenously; or (b) deslorelin injection (prepared by 1 of

From the Department of Clinical Sciences, Colorado State University, Fort Collins, CO.
Reprint requests to: P.M. McCue, 3194 Rampart Road, Ft. Collins, CO 80523.
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Table 1. Comparison of follicle diameter and edema score at time of treatment; interval to ovulation; and percentage of mares ovulating within 48 hours after administration of 1 of 2 compounded products containing 1.5 mg deslorelin

Group	(n)	Follicle Diameter (mm)	Edema Score	Interval to Ovulation (days)	% Ovulation within 48 hr
Deslorelin[a]	21	39.7 ± 3.4	1.4 ± 0.8	1.9 ± 0.5	85.7%
Deslorelin[b]	80	40.5 ± 2.9	1.6 ± 0.8	1.9 ± 0.5	91.3%

[a] Applied Pharmacy Services, Mobile, AL.

[b] Essential Pharmaceuticals, Omaha, NE.

2 compounding pharmacies) at a dose of 1.5 mg, administered intramuscularly. One of the deslorelin products (Applied Pharmacy Services, Mobile, AL) was lyophilized and reconstituted to 1.5 mg/ml with sterile saline, and the other deslorelin product (Essential Pharmaceuticals, Omaha, NE) was provided as a solution containing 1.5 mg deslorelin per milliliter. Nineteen additional mares were administered a saline placebo (1.0 ml volume) intravenously and monitored for interval from placebo treatment to ovulation.

Differences between groups for age, follicle diameter, edema score, and interval from treatment to ovulation were determined by 1-way analysis of variance using a commercial statistical software package (SAS, version 8.0, SAS Institute Inc., Cary, NC). Tukey-Kramer HSD test was used when significant group effects were observed. Percentages of mares that ovulated within 48 hours after treatment were compared using Fisher's exact test or chi-square analysis. Intervals from prostaglandin to ovulation in mares induced to ovulate with either hCG or deslorelin were also compared to determine whether the use of injectable deslorelin was associated with a prolonged interovulatory period as had been reported for an implant form of deslorelin (Ovuplant™; Fort Dodge Animal Health, Inc., Fort Dodge, KS). Data are presented as the mean ± standard deviation, and values were considered to be significantly different at $P < .05$.

RESULTS

Data from 248 estrous cycles fit the criteria for inclusion in this study. Efficacy at inducing a timed ovulation was first compared between the groups of mares receiving one of the two compounded deslorelin products. No significant differences ($P > .05$) were seen between follicle diameter or edema score at time of treatment, interval to ovulation, or percentage of mares that ovulated within 48 hours after treatment (Table 1). Data for mares receiving the two deslorelin products were subsequently pooled for comparison with hCG.

Average age of mares administered a saline placebo was significantly less (6.6 ± 1.7 years) than that of mares receiving hCG (10.5 ± 5.0 years) or deslorelin (13.0 ± 6.3 years) ($P < .05$). There was a significant difference in average age between mares receiving deslorelin (13.0 ± 0.5 years) and those receiving hCG (10.5 ± 0.5 years) ($P < .05$).

The average follicle diameter at the time of hormone or saline placebo treatment was similar ($P > .05$) between groups (Table 2). Interval to ovulation was shorter, and the percentage of mares that ovulated within 48 hours of treatment was greater, in mares receiving an ovulation-inducing agent than in mares receiving a saline placebo ($P < .05$). There was no significant difference in the interval from treatment to ovulation or the percentage of mares ovulating within 48 hours between hormone treatment groups ($P > .05$) (Table 2).

Failure of ovulation within 48 hours after administration of an ovulation-inducing agent occurred in 24 of the 248 cycles (9.7%). This included 15 mares (11.7%) treated with hCG and 9 mares (8.9%) treated with deslorelin.

A total of 140 mares received hCG during the 2006 breeding season. Some mares were treated during cycles when their dominant follicle was <35 or >45 mm in diameter, and those cycles are therefore not represented in Table 2. Fifteen mares were administered a second dose of hCG during a subsequent cycle in the same breeding season. No mare was administered hCG more than twice during the season. The intervals from hCG administration to ovulation were 1.9 ± 0.7 and 2.1 ± 1.0 days, respectively, for the first and second treatments ($P > .05$).

A total of 118 mares received deslorelin during the 2006 breeding season. Again, some mares were treated when follicles were either <35 or >45 mm in diameter, and data from those cycles are not included in Tables 1 or 2. In many instances, mares were administered deslorelin during more than 1 estrous cycle during the breeding season. No significant differences ($P > .05$) were seen in interval from treatment to ovulation or percentage of mares ovulating within 48 hours after treatment for mares receiving deslorelin during more than 1 estrous cycle (Table 3).

Mares induced to ovulate with hCG (n = 17 cycles) or deslorelin (n = 30 cycles) and subsequently administered prostaglandins after an embryo collection attempt had prostaglandin-to-ovulation intervals of 11.2 ± 1.4 and 10.7 ± 1.9 days, respectively ($P > .05$). Deslorelin was administered to 17 mares ≥20 years of age over a total of 25 estrous cycles, and the average interval to ovulation and percentage of mares ovulating within 48 hours were 1.9 ± 0.4 and 96%, respectively.

DISCUSSION

A basic understanding of ovulation-inducing agents and the mechanism by which they stimulate ovulation is important when making a clinical decision. Deslorelin is a synthetic agonist of the natural peptide hormone GnRH.